UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,760	09/29/2003	Mark McCormick	700706.90203	1470

26734 7590 10/02/2007

QUARLES & BRADY LLP
33 E. MAIN ST, SUITE 900
P.O. BOX 2113
MADISON, WI 53701-2113

EXAMINER	
HANDY, DWAYNE K	
ART UNIT	PAPER NUMBER
1743	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,760	MCCORMICK ET AL	
	Examiner	Art Unit	
	Dwayne K. Handy	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7 and 9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 5-7 and 9-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-17 of copending Application No. 10/674,758. Although the conflicting claims are not identical, they are not patentably distinct from each other. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 5-7 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Butler et al. (6,589,726). The Examiner believes Applicant is familiar with the Butler reference. This rejection was applied and upheld in previous Office Actions. It remains in effect. Please see Response to Arguments below.

Response to Arguments

5. Applicant's arguments filed 3/21/07 have been fully considered but they are not persuasive. Applicant has argued that Butler does not teach synthesizing probes and depositing hydrophobic barriers with the same instrument – a maskless array synthesizer instrument. Applicant has also requested that Applicant show this teaching in Butler. Applicant has noted the passage from columns 7 and 8 as well as Example 2. The Examiner directs Applicant to column 10, line 13 – column 11, line 61.

> (26) In addition to the use of photoresist in generating patterned hydrophilic and hydrophobic sites, **surface tension arrays may be fabricated without the use of photoresist.** For example, a solid support may be first reacted with a reagent to form hydrophilic sites. The hydrophilic sites may then be reacted in selected areas. The remaining hydrophilic sites may then be reacted with a reagent to form hydrophobic sites. The protected hydrophilic sites may then be deprotected to anchor in situ synthesis or

to deposit chemical or biological entities. For example, a glass surface may be first reacted with a reagent to generate free hydroxyl or amino sites. These hydrophilic sites may be reacted with a protected nucleoside coupling reagent or a linker to protect selected hydroxyl or amino sites. A protected nucleotide coupling reagent includes, for example, a DMT-protected nucleoside phosphoramidite, DMT-protected H-phosphonate, etc. A linker may be of six or more atoms in length. The unprotected hydroxyl or amino sites may then be reacted with a reagent, for example, perfluoroalkanoyl halide, to form hydrophobic sites inert to in situ polynucleotide synthesis. The protected hydrophilic sites may be deprotected to anchor in situ polynucleotide synthesis. Variations of these procedures may also be used to fabricate a solid support surface such that solution of chemical or biological entities at a derivatized site is spatially separated from solutions of chemical or biological entities at other derivatized sites.

(27) In Situ Synthesis or Spotting of Presynthesized Compounds

(28) **Solutions of reactants may be added to hydrophilic sites on the surface using the "drop-on-demand" method, which is analogous to the ink-jet printing technology. This approach typically utilizes piezoelectric or other forms of propulsion to transfer reagents from miniature nozzles to solid surfaces. For example, a printer head** may travel across the array, and at each spot, electric field contracts, forcing a microdroplet of reagents onto the array surface. The drop-on-demand technology allows high-density gridding of virtually any reagents of interest. It is also easier using this method to take advantage of the extensive chemistries already developed for polynucleotide synthesis, for example, flexibility in sequence designs, synthesis of polynucleotide analogs, synthesis in the 5'-3' direction, etc. Because ink jet technology does not require direct surface contact, piezoelectric delivery is amendable to very high throughput.

(29) A piezoelectric pump may be used to add reagents to the in situ synthesis. Microdroplets of 50 picoliters to 2 microliters of reagents may be delivered to the array surface. The design, construction, and mechanism of a piezoelectric pump are described in U.S. Pat. Nos. 4,747,796 and 5,985,551. The piezoelectric pump may deliver minute droplets of liquid to a surface in a very precise manner. For example, a picopump is capable of producing picoliters of reagents at up to 10,000 Hz and accurately hits a 250 micron target at a distance of 2 cm.

(30) The reactions at the hydrophilic sites may form covalent bonds such as esters or amide bonds or may involve non-covalent specific binding reactions such as antibody/antigen binding or base pairing. In some embodiments, the growing polynucleotides are attached to the solid support via an intervening linker moiety. The linker moiety may be of six or more atoms in length. Convention solid phase polynucleotide synthesis is well known in the art of polynucleotide synthesis. See, e.g., Protocols for Oligonucletides and Analogs; Agrawal, S., Ed.; Hurnana Press: Totowa, N.J., (1993). As used in the instant invention, the terms polynucleotides/nucleotides (often referred to as oligonucleotides, primers, probes, nucleic acids, etc) refer to naturally occurring polynucleotides/nucleotides, e.g., DNA or RNA. These terms also refer to modified/protected forms thereof or analogs of naturally occurring polynucleotides. The synthesis of many modified or unnatural polynucleotides is well known in the art. See, e.g., Verma et al., Annu. Rev. Biochem. 67:99-134 (1998), Venkatesan et al. J. of Org. Chem., 61:525-529 (1996), Kahl et al., J. of Org. Chem., 64:507-510 (1999), and Kahl et al., J. of Org. Chem. 63:4870-4871 (1998), and U.S. Pat. Nos. 5,739,386, 5,700,642 and 5,830,655. The modification of polynucleotides may be located at polynucleotide bases, sugars or backbone. For example, polynucleotides containing a modified 3'-5' internucleotide linkage in place of one of the phosphodiester groups, such as ribose, dialkoxysilane, phosphorothioate, and phosphoramidate internucleotide linkage may be synthesized. In addition, the naturally occurring nucleic acids have 3'-5' phosphodiester linkage may be replaced with 2'-5' linkage.

(31) The highly charged phosphodiesters in natural nucleic acid backbone may be replaced by neutral sugar phosphate backbone analogues. For example, phosphotriesters in which the oxygen that is normally charged in natural nucleic acids is esterified with an alkyl group may be used. Another class of backbone analogs is polypeptide nucleic acids (PNAs), in which a peptide backbone is used to replace

the phosphodiester backbone. PNAs are capable of forming sequence-specific duplexes that mimic the properties of double-strand DNA except that the complexes are completely uncharged. See, e.g., Giesen, U. et al., Nucleic Acids Research 26(21):5004-5006 (1998); Good, L., et al., Nature Biotechnology 16:355-358 (1998); and Nielsen, P., Current Opinion in Biotechnology 10:71-75 (1999).

(32) Modifications of bases and sugars may include a substituent on or replacement of one of the bases or sugars, such as 7-deazaguanosine, 5-methylcytosine, 2,6-diamino purine, 5-bromouridine, 5-Chlorouridine, inosine, uridine, and the like.

(33) In some embodiments, the modified polynucleotides may contain a cleavage site. The cleavage methods may include a variety of enzymatic, or non-enzymatic means, such as chemical, thermal, photolytic cleavage, or a combination thereof. For example, the polynucleotides may include a photocleavable linker, such as orthonitrobenzyl class of photocleavable linkers. The cleavable sites contained within the modified polynucleotides may include chemically cleavable groups, such as dialkoxysilane, 3'-(S)-phosphorothioate, 5'-(S)-phosphorothioate, 3'-(N)-phosphoramidate, 5'-(N)-phosphoramidate, and ribose.

This passage details the use of the "drop on demand" method mentioned by Applicant. It includes the step of depositing a hydrophobic material in the form of phosphoramidite on the substrate having the probes or molecules. Butler teaches the use of either a printer head or other piezoelectric dispenser to dispense all reagents (column 10). Therefore, the Examiner fails to see how Butler does not teach the same instrument to deposit the probes, reagents and hydrophobic material.

6. Applicant has then argued that Butler does not provide technical direction on the placement of probes and arrangement of the probes prior to the deposition of the hydrophobic barrier. This argument is beyond the scope of the claim as written. The Examiner notes that Applicant has not specified any structure to the barrier other than to recite a "hydrophobic barrier which surrounds each subarray. Applicant has not specified that each site or each probe on the array be surrounded by the hydrophobic barrier. Applicant has not claimed a particular arrangement of probes and barriers other than the selection of subarrays that are surrounded by hydrophobic barriers. The

Examiner submits that any two probes of a larger array constitutes a subarray. For example, a probe array comprised of 200 sites may be grouped into two 100-site "subarrays". Depositing the phosphoramidite material into any or all of the outer sites of either subarray would form a barrier that surrounds each subarray. This is what the claim as written requires. In short, the Examiner takes the position that the deposition of a hydrophobic material – the phosphoramidite material – onto the substrate holding the array would inherently provide a hydrophobic barrier surrounding each subarray since the material is hydrophobic and would prevent mixing with hydrophilic materials (i.e. a barrier between each array). Applicant seems to be arguing that Butler's mere deposition of hydrophobic material on the substrate to form a "barrier" is excluded and/or does not meet the claim as written. The Examiner respectfully disagrees given the breadth of the claim as currently written.

7. Applicant has also argued that the while the disclosure of the '768 application mentions hydrophobic barriers, the claims of the instant claim are distinct from the those of '768 since '768 is directed to loading samples (page 5, line 28 – page 6, line 2). The Examiner respectfully disagrees. The Examiner considers the depositing of a sample ('758) to be within the scope of selecting and synthesizing a probe set (instant claims). In addition, Applicant clearly recites the hydrophobic barrier of phosphoramidite in claim 16.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dwayne K. Handy whose telephone number is (571)-272-1259. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DKH
September 30, 2007

Jill Warden
Supervisory Patent Examiner
Technology Center 1700